

WHAT IS CLAIMED:

1. A method of ablating or killing normal, benign hyperplastic, and cancerous prostate epithelial cells comprising:
  - 5 providing a biological agent which binds to an extracellular domain of prostate specific membrane antigen and
  - 10 contacting said cells with the biological agent under conditions effective to permit both binding of the biological agent to the extracellular domain of the prostate specific membrane antigen and ablating or killing of said cells.
- 15 2. A method according to claim 1, wherein the biological agent is an antibody or binding portion thereof, probe, or ligand.
- 20 3. A method according to claim 1, wherein the biological agent is internalized with the prostate specific membrane antigen.
- 25 4. A method according to claim 1, wherein said contacting is carried out in a living mammal and comprises:
  - 30 administering the biological agent to the mammal under conditions effective to permit both binding of the biological agent to the extracellular domain of the prostate specific membrane antigen and killing of said cells.
- 35 5. A method according to claim 4, wherein the biological agent is internalized with the prostate specific membrane antigen.
6. A method according to claim 4, wherein said administering is carried out orally, parenterally,

subcutaneously, intravenously, intramuscularly, intraperitoneally, by intranasal instillation, by intracavitory or intravesical instillation, intraocularly, intraarterially, intralesionally, or by 5 application to mucous membranes.

7. A method according to claim 2, wherein an antibody is used in carrying out said method, the antibody being selected from the group consisting of a 10 monoclonal antibody and a polyclonal antibody.

8. A method according to claim 7, wherein the antibody is selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody. 15

9. A method according to claim 7, wherein the antibody is a monoclonal antibody produced by a hybridoma cell line having an ATCC Accession Number selected from the group consisting of HB-12101, HB-12109, HB-12127, and 20 HB-12126.

10. A method according to claim 2, wherein a binding portion of an antibody is used in carrying out said method, the binding portion being selected from the 25 group consisting of an Fab fragment, an  $F(ab')_2$  fragment, and an Fv fragment.

11. A method according to claim 2, wherein the probe or ligand is used in carrying out said method. 30

12. A method according to claim 1, wherein the biological agent is bound to a substance effective to kill or ablate said cells upon binding of the biological agent to the extracellular domain of the prostate 35 specific membrane antigen of said cells.

13. A method according to claim 12, wherein the substance effective to kill said cells is a cytotoxic drug.

5 14. A method according to claim 13, wherein the cytotoxic drug is selected from the group consisting of therapeutic drug, a compound emitting radiation, molecules of plant, fungal, or bacterial origin, biological proteins, and mixtures thereof.

10 15. A method according to claim 2, wherein the antibody is effective to initiate an endogenous host immune function.

15 16. A method according to claim 15, wherein the endogenous host immune function is complement-mediated cellular cytotoxicity.

20 17. A method according to claim 15, wherein the endogenous host immune function is antibody-dependent cellular cytotoxicity.

25 18. A method according to claim 1, wherein the biological agent is in a composition further comprising a physiologically acceptable carrier, excipient, or stabilizer.

30 19. A method according to claim 1, wherein the biological agent is in a composition further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

20. A method according to claim 1 further comprising:

providing a second biological agent which binds to the extracellular domain of prostate specific membrane antigen and

5 contacting said cells with the second biological agent under conditions effective to permit binding of the second biological agent to the extracellular domain of the prostate specific membrane antigen.

10 21. A method according to claim 20, wherein the biological agent and the second biological agent bind to non-competing binding sites on the extracellular domain of the prostate specific membrane antigen.

15 22. A method according to claim 20, wherein the biological agent is a J415 monoclonal antibody and the second biological agent is an E99, a J533, or a J591 monoclonal antibody.

20 23. A method according to claim 20, wherein the biological agent is bound to a substance effective to kill or ablate said cells upon binding of the biological agent to the extracellular domain of the prostate specific membrane antigen of said cells and upon 25 activation by an activator and wherein the second biological agent is bound to the activator.

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*b5* 24. A method of detecting normal, benign hyperplastic, and cancerous prostate epithelial cells or a portion thereof in a biological sample comprising:

providing an biological agent which binds to an extracellular domain of prostate specific membrane antigen, wherein the biological agent is bound to a label effective to permit detection of said cells or a portion

thereof upon binding of the biological agent to said cells or a portion thereof;

5       contacting the biological sample with the biological agent having a label under conditions effective to permit binding of the biological agent to the extracellular domain of the prostate specific membrane antigen of any of said cells or a portion thereof in the biological sample; and

10      detecting a presence of any of said cells or a portion thereof in the biological sample by detecting the label.

25. A method according to claim 24, wherein the biological agent is an antibody or binding portion thereof, probe, or ligand.

*Sub B4*      26. A method according to claim 24, wherein the biological agent is internalized with the prostate specific membrane antigen.

20           27. A method according to claim 24, wherein said contacting is carried out in a living mammal and comprises:

25           administering the biological agent to the mammal under conditions effective to permit binding of the biological agent to the extracellular domain of the prostate specific membrane antigen of any of said cells or a portion thereof in the biological sample.

30           4. A method according to claim 27, wherein the label is a short-range radiation emitter.

5. A method according to claim 27, wherein said detecting is carried out rectally.

6 30. A method according to claim 27, wherein  
the biological sample is the mammal's prostatic fossa.

7 31. A method according to claim 27, wherein  
5 said detecting is carried out after a prostatectomy.

32. A method according to claim 27, wherein  
the biological agent is internalized with the prostate  
specific membrane antigen.

10 9 33. A method according to claim 27, wherein  
said administering is carried out orally, parenterally,  
subcutaneously, intravaneously, intramuscularly,  
intraperitoneally, by intravascular instillation, by  
15 intracavitory or intravesical instillation,  
intraocularly, intraarterially, intralesionally, or by  
application to mucous membranes.

20 34. A method according to claim 25, wherein an  
antibody is used in carrying out said method, said  
antibody being selected from the group consisting of a  
monoclonal antibody and a polyclonal antibody.

25 11 35. A method according to claim 24, wherein  
the antibody is selected from the group consisting of an  
E99, a J415, a J533, and a J591 monoclonal antibody.

30 12 36. A method according to claim 24, wherein  
the antibody is a monoclonal antibody produced by a  
hybridoma cell line having an ATCC Accession Number  
selected from the group consisting of HB-12101, HB-12109,  
HB-12127, and HB-12126.

35 37. A method according to claim 25, wherein a  
binding portion of an antibody is used in carrying out

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said method, the binding portion being selected from the group consisting of an Fab fragment, an  $F(ab')_2$  fragment, and an Fv fragment.

5 38. A method according to claim 25, wherein a probe or ligand is used in carrying out said method.

*14* 29. A method according to claim 24, wherein the label is selected from the group consisting of a 10 fluorescent label, a radioactive label, a nuclear magnetic resonance active label, a luminescent label, and a chromophore label.

15 40. A method according to claim 24, wherein the biological agent is in a composition further comprising a physiologically acceptable carrier, excipient, or stabilizer.

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20 41. A method according to claim 24, wherein the biological agent is in a composition further comprising a pharmaceutically acceptable carrier, excipient, or stabilizer.

*17* 25 42. A method according to claim 24, wherein said contacting is carried out in a sample of serum or urine.

30 43. An isolated biological agent which binds to an extracellular domain of prostate specific membrane antigen.

35 44. An isolated biological agent according to claim 43, wherein said isolated biological agent is an isolated antibody or binding portion thereof, probe, or ligand.

45. An isolated biological agent according to claim 43, wherein the biological agent is internalized with the prostate specific membrane antigen.

5 46. An isolated biological agent according to claim 44, wherein the isolated biological agent is an antibody selected from the group consisting of a monoclonal antibody and a polyclonal antibody.

10 47. An isolated biological agent according to claim 46, wherein the antibody is selected from the group consisting of an E99, a J415, a J533, and a J591 monoclonal antibody.

15 48. An isolated biological agent according to claim 46, wherein the antibody is a monoclonal antibody produced by a hybridoma having an ATCC Accession Number selected from the group consisting of HB-12101, HB-12109, HB-12127, and HB-12126.

20 49. An isolated biological agent according to claim 44, wherein the isolated biological agent is a binding portion of an antibody selected from the group consisting of a Fab fragment, a  $F(ab')_2$  fragment, and a Fv fragment.

25 50. An isolated biological agent according to claim 44, wherein the isolated biological agent is a probe or ligand.

30 51. An isolated biological agent according to claim 43, wherein the biological agent is bound to a cytotoxic drug.

52. An isolated biological agent according to  
claim 51, wherein the cytotoxic drug is selected from the  
group consisting of a therapeutic drug, a compound  
emitting radiation, molecules of plant, fungal, or  
5 bacterial origin, biological proteins, and mixtures  
thereof.

10 53. A composition comprising:  
a biological agent according to claim 51 and  
a physiologically acceptable carrier,  
excipient, or stabilizer mixed with the biological agent.

15 54. A composition comprising:  
a biological agent according to claim 51 and  
a pharmaceutically acceptable carrier,  
excipient, or stabilizer mixed with the biological agent.

20 55. An isolated biological agent according to  
claim 43, wherein said biological agent is bound to a  
label.

25 56. An isolated biological agent according to  
claim 55, wherein the label is selected from the group  
consisting of a fluorescent label, a biologically-active  
enzyme label, a radioactive label, a nuclear magnetic  
resonance active label, a luminescent label, and a  
chromophore label.

30 57. A composition comprising:  
a biological agent according to claim 55 and  
a physiologically acceptable carrier,  
excipient, or stabilizer mixed with the biological agent.

58. A composition comprising:  
a biological agent according to claim 55 and  
a pharmaceutically acceptable carrier,  
excipient, or stabilizer mixed with the biological agent.

5 59. A kit for detecting prostate cancer  
comprising:  
a biological agent according to claim 55 and  
means to detect the label.

10 60. A kit according to claim 59, wherein the  
label is selected from the group consisting of a  
fluorescent label, a biologically-active enzyme label, a  
radioactive label, a nuclear magnetic resonance active  
15 label, a luminescent label, and a chromophore label.

20 61. A kit according to claim 59, wherein said  
biological agent is an E99, a J415, a J533, or a J591  
monoclonal antibody.

25 62. A kit according to claim 59, wherein the  
biological agent is in a composition further comprising a  
physiologically acceptable carrier, excipient, or  
stabilizer.

30 63. A kit according to claim 59, wherein the  
biological agent is in a composition further comprising a  
pharmaceutically acceptable carrier, excipient, or  
stabilizer.

64. A hybridoma cell line that produces a  
monoclonal antibody which binds to an extracellular  
domain of prostate specific membrane antigen.

65. A hybridoma cell according to claim 64, wherein the antibody is internalized with the prostate specific membrane antigen.

5 66. A hybridoma cell line according to claim 64, wherein the monoclonal antibody is an E99, a J415, a J533, or a J591 monoclonal antibody.

10 67. A hybridoma cell line according to claim 64 wherein the hybridoma cell line has an ATCC Accession Number selected from the group consisting of HB-12101, HB-12109, HB-12127, and HB-12126.

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